Perceived Risks of Participating in HIV Cure-Related Research in the United States

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Background

Since most HIV cure research strategies are proof-of-concept experiments, they are associated with significant potential risks. We investigated perceptions of risks in HIV cure clinical research in the United States. We hypothesized that perceived clinical risks, including study procedures, side effects, and social risks, affect willingness to participate in research.

Methods

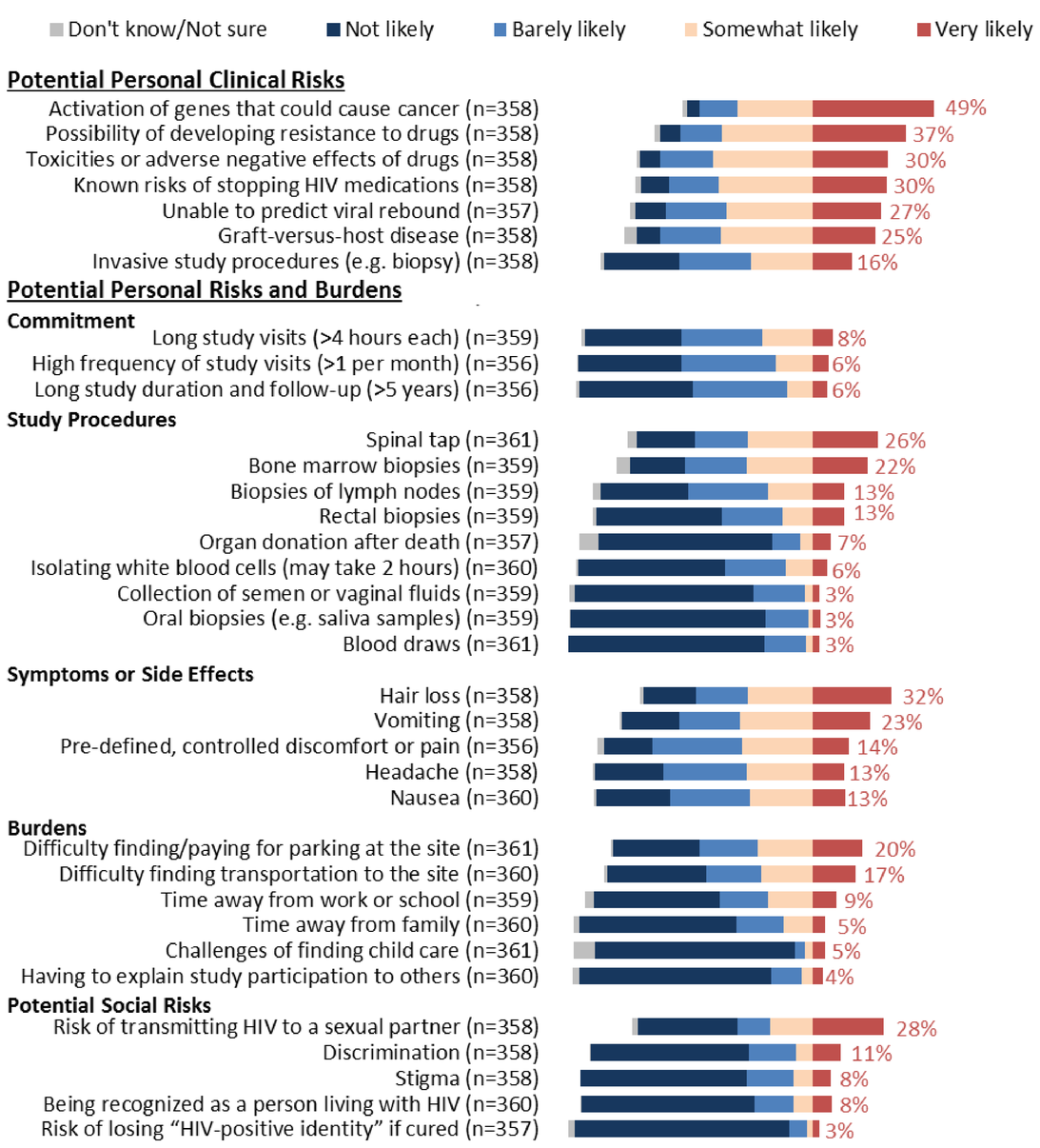
We implemented a cross-sectional survey with 400 American adults living with HIV (22% female; 77% male; <1% transgender) in 2015. The sample was ethnically diverse (65% Caucasian, 17% African-American, 12% Hispanic, 4% mixed and 2% Asian). Most U.S. states were represented. We also conducted extensive key informant interviews with 36 people living with HIV, as well as numerous researchers, bioethicists, members of IRBs and regulatory agencies to assess perceptions of risks related to HIV cure studies.

Results

Increased cancer risk (49% [95% CI: 42, 52%]; n = 358), developing resistance to ARVs (37% [32, 42%]; n = 358), toxicities (30% [25, 35%]; n = 358) and known risks of stopping HIV medications (30% [25, 35%]; n = 358) were the potential clinical risks most likely to discourage participation. Procedures presenting the greatest barriers were lumbar punctures (26%), bone marrow biopsies (22%), lymph node biopsies (13%), and rectal biopsies (13%). The burden category shows that we should not underestimate the importance of addressing possible obstacles to study participation, such as transportation or parking. Risk of transmitting HIV in case of unsuspected viral rebound (28% [23, 33%]; n = 358) was the most concerning potential social risk to participation. The need for intense commitment did not appear to be a strong deterrent in the survey, but emerged in the key informant interviews as a possible deterrent to participation.

The study showed that the greater the risks, the more likely potential volunteers are deterred from participating in research.

Likelihood of Factors to Discourage Considering Participation in HIV Cure-Related Studies



Percentages reflect "Very likely to discourage". The remainder (up to 100%) includes the sum of "Somewhat likely to discourage", "Barely likely to discourage", "Not likely to discourage" and "Don't know/Not sure".

Around 10% of survey respondents answered "None" or "Not Sure" to the question: "What other potential risks are "very likely to discourage" you from participating in an HIV cure-related study?." These potential volunteers did not place any upper limits on acceptable risks. **This result underscores the need for robust education efforts around possible risks of HIV cure-related research participation in the United States.**

Results (continued)

In the key informant interviews, risks discouraging participation included various clinical risks such as developing resistance to antiretroviral drugs (ARVs), cancer, procedure-related risks, side effects, pain, debilitation, irreversible harm or death, scientific uncertainty, and failure to achieve a cure. Dissuading financial risks included loss of disability insurance or employment. Potential social risks included disclosure of HIV status or breach of confidentiality, stigma/discrimination, poor treatment by research staff, transmitting HIV to others, employment loss, and media attention.

Perceptions of risks in HIV cure clinical studies differed significantly between clinician-researchers, patient-participants and policy-makers in the qualitative analysis. Clinician-researchers had expert knowledge about possible medical or clinical risks of HIV cure research, including those associated with specific research modalities or investigational interventions included in informed consent forms. Clinician-researchers were adamant about the imperative to reduce or mitigate risks whenever possible. They also cautioned about the need to be careful in interpreting risk information, such as side effects of the compounds, especially in the context of the disease for which they have been previously approved or re-purposed. Policy-makers/regulators were rather comfortable reciting possible risks of HIV cure research; however, they were more concerned with normative categories of risks, such as known versus unknown risks, short-term versus long-term risks and real versus theoretical risks. Patient-participants are the only category of informants to have discussed possible social risks related to HIV cure research participation. Patient-participants also perceived emotional and financial risks related to HIV cure research participation, including concerns around maintaining disability insurance or income (including private or Social Security), current health care or insurance coverage. Overall, key informants stated that the perceived riskiest HIV cure research modalities included stem cell transplants/gene therapy, latency-reversing agents, and combination approaches.

Conclusions

Understanding perceptions of risks is important to inform study design, informed consent, and recruitment and retention strategies for HIV cure-related research. HIV cure clinical researchers should minimize risks to study participants while maximizing scientific knowledge gained. Risk perceptions can play a major role in determining what HIV cure research study gets approved or moved forward and in decisions about whether to participate. Community and participant confidence regarding the safety of a scalable cure should be a compelling driver for discovery and progress towards a cure.

Recommendations

- ✓ HIV cure clinical investigators have an ethical duty to convey risks to potential study participants. Risks must be minimized and they must be reasonable in relation to the importance of the research knowledge that may be generated. Ethical guidelines must continue to protect study participants against unacceptable risks.
- ✓ It is important to differentiate the risks that stem from investigational interventions or agents, study visit procedures, and risk monitoring, and understand how deviations from standards of care (e.g. analytical treatment interruption) can add to the actual and perceived risks.
- ✓ The heterogeneity of HIV cure clinical studies and the scientific uncertainty make the reliability of risk-benefit judgement difficult. We emphasize prudence in exposing "otherwise healthy subjects" to substantial likelihood of serious risks.
- ✓ HIV cure clinical investigators need to minimize risks to study participant to prevent crises of confidence in the HIV cure clinical research enterprise, because this could set the field back several years. HIV cure clinical investigators should also ensure that data points derived from HIV cure research participation are as valid and informative as possible so as to move the scientific field forward and are justified when compared with the risks taken by study participants.
- ✓ It is important to remember that potential volunteers' perceptions of risks may sometimes differ from expert scientific opinions. There should be sustained education efforts around HIV cure research for potential volunteers.
- ✓ More formative research is needed on actual and perceived risks of participating in HIV cure clinical studies. Attention should also be devoted to risk communication and evaluating future risks, such as cancer several years after study participation has ended. Social harms should also be captured as part of HIV cure clinical research participation.

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